



## **Depressive symptoms in women's midlife in relation to their body weight before, during and after childbearing years**

Bliddal, Mette; Pottegård, Anton; Kirkegaard, Hans; Olsen, J; Sørensen, T I A; Nohr, E A

*Published in:*  
Obesity Science & Practice

*DOI:*  
[10.1002/osp4.75](https://doi.org/10.1002/osp4.75)

*Publication date:*  
2016

*Document version*  
Publisher's PDF, also known as Version of record

*Document license:*  
[CC BY-NC-ND](#)

*Citation for published version (APA):*  
Bliddal, M., Pottegård, A., Kirkegaard, H., Olsen, J., Sørensen, T. I. A., & Nohr, E. A. (2016). Depressive symptoms in women's midlife in relation to their body weight before, during and after childbearing years. *Obesity Science & Practice*, 2(4), 415-425. <https://doi.org/10.1002/osp4.75>

## ORIGINAL ARTICLE

# Depressive symptoms in women's midlife in relation to their body weight before, during and after childbearing years

M. Bliddal<sup>1,2,3</sup>, A. Pottegård<sup>4</sup>, H. Kirkegaard<sup>1</sup>, J. Olsen<sup>5</sup>, T. I. A. Sørensen<sup>6,7,8</sup> and E. A. Nohr<sup>1,2</sup>

<sup>1</sup>Institute of Clinical Research, Research Unit of Gynaecology and Obstetrics, University of Southern Denmark, Odense, Denmark; <sup>2</sup>Department of Gynaecology and Obstetrics, Odense University Hospital, Odense, Denmark; <sup>3</sup>OPEN – Odense Patient data Explorative Network, Odense University Hospital, Odense, Denmark; <sup>4</sup>Clinical Pharmacology, Department of Public Health, University of Southern Denmark, Odense, Denmark; <sup>5</sup>Department of Public Health, Section for Epidemiology, Aarhus University, Aarhus, Denmark; <sup>6</sup>Novo Nordisk Foundation Center for Basic Metabolic Research, University of Copenhagen, Copenhagen, Denmark; <sup>7</sup>Institute of Preventive Medicine, Bispebjerg and Frederiksberg Hospitals – Part of Copenhagen University Hospital, Copenhagen, Denmark; <sup>8</sup>MRC Integrative Epidemiology Unit, Bristol University, Bristol, UK;

Received 23 August 2016; revised 16 September 2016; accepted 17 September 2016

Address for correspondence: M Bliddal, Department of Gynaecology and Obstetrics, Odense University Hospital, Klørvænget 10, 10th sal, indgang 112, 5000 Odense C, Denmark. E-mail: mette.bliddal@rsyd.dk

## Summary

### Objective

This study aimed to examine how weight and weight changes related to pregnancy were associated with depressive symptoms 11–16 years after childbirth.

### Method

We followed 16,998 first-time mothers from the Danish National Birth Cohort up till 16 years after birth and estimated associations between depressive symptoms and pre-pregnancy body mass index (BMI) ( $\text{kg m}^{-2}$ ), weight changes in different time periods, and BMI-adjusted waist circumference 7 years after birth ( $\text{WC}_{\text{BMI}}$ , cm). Depressive symptoms were estimated by the Center for Epidemiologic Studies Depression 10-item scale. Multiple logistic regression analyses were used to estimate odds ratios (OR) and 95% confidence intervals.

### Results

Compared with normal-weight, we found that underweight, overweight and obesity were associated with greater odds of depressive symptoms (1.29, 1.24 and 1.73, respectively). Compared with weight change  $\pm 1$  BMI unit during the total follow-up period, greater odds for depressive symptoms were observed with weight loss (OR 1.14, 0.96–1.36) or gain of  $2\text{--}2.99 \text{ kg m}^{-2}$  (OR 1.11, 0.92–1.33) or gain of  $\geq 3 \text{ kg m}^{-2}$  (OR 1.68, 1.46–1.94).  $\text{WC}_{\text{BMI}} > 2.2$  cm was associated with greater odds of depressive symptoms (OR 1.16, 0.99–1.36) than waist circumference as predicted by BMI.

### Conclusion

Low and high pre-pregnancy BMI, weight changes and  $\text{WC}_{\text{BMI}}$  larger than predicted were associated with more depressive symptoms in midlife.

**Keywords:** Body mass index, body-weight changes, depressive symptoms, maternal health.

## Introduction

Obesity is a growing public health problem worldwide (1), also among women of childbearing age. In 2015, 27% of Danish women were overweight when entering pregnancy: of these, 12% were categorized as having obesity (2). The reported prevalence of mental illness is increasing, and it is estimated that mental disorders – primarily depression – account for 20% of the disease burden in the European Union (3). Obesity has been linked with depression, both in the general population (4–9) and among new mothers (10,11). Weight changes may also

be associated with later depression, although evidence is inconsistent (8,12,13).

For women, the childbearing period is characterized by steep weight gain during pregnancy followed by rapid weight loss. For some mothers, pregnancy induces a lasting weight gain, either as postpartum weight retention or as weight gain in early motherhood, possibly because of changes in lifestyle (14,15), all of which increases the risk of later overweight or obesity (16,17). Also, postpartum depression may influence long-term obesity as depression may negatively affect the natural weight loss after childbirth (18). Both a woman's pre-pregnancy body mass

index (BMI) and these pregnancy-related weight changes may be linked with depression through both physical and mental mechanisms such as dys-regulation of the hypothalamic–pituitary–adrenal axis, inflammation, the metabolic syndrome, and poor self-esteem and stigma (5,19). Low pre-pregnancy BMI and postpartum weight changes (both gain and loss) have been associated with long-term risk of anxiety and depressive disorders leading to prescriptions of antidepressants or hospital diagnoses in the time up till 6 years postpartum (13). On the other hand, many women suffer from depressive symptoms (20), which might also lead to obesity and weight changes through altered lifestyle habits (19).

Finally, pregnancy is associated with a change in body composition with an increase in adipose tissue in the visceral compartment (21). Abdominal fat is more metabolically active than fat tissue in general and have been associated with depression (4,22,23). Underlying factors could include unhealthy eating habits or increased levels of cytokines (4,24,25). This association has not been investigated in any of the previous studies.

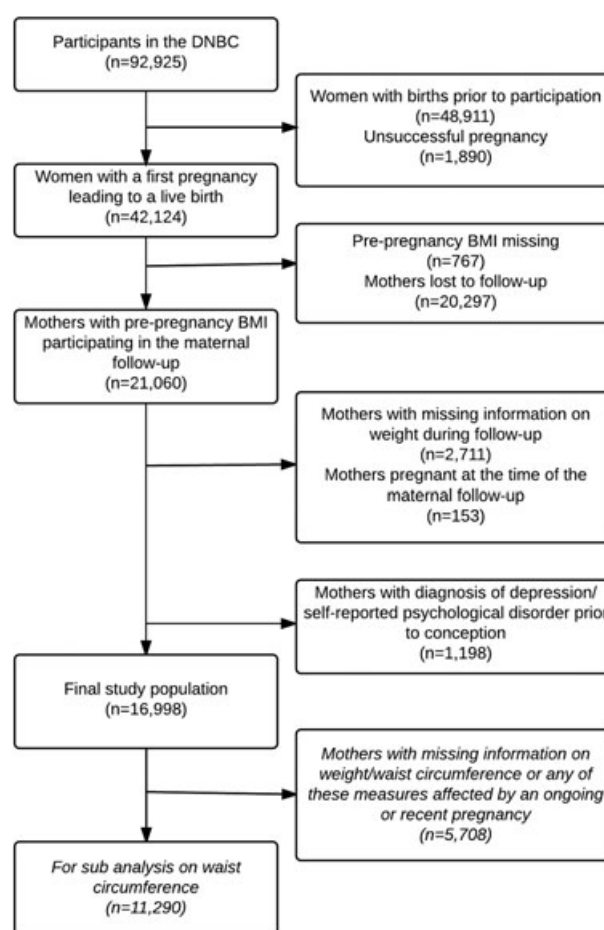
The aim of this study was to investigate if pre-pregnancy BMI and body weight changes during and after years of childbearing relate to depressive symptoms in midlife, measured 11–16 years after a woman's first birth. Additionally, we studied if waist circumference (WC) adjusted for BMI ( $WC_{BMI}$ ) 7 years after childbirth, as an indicator for abdominal adiposity, was associated with depressive symptoms. We hypothesized that high pre-pregnancy BMI, weight changes in the years of reproduction and beyond, and abdominal obesity were associated with the prevalence of depressive symptoms in mothers in midlife.

## Methods

This study is based on the Danish National Birth Cohort (DNBC), which contains self-reported and healthcare-recorded information on health and lifestyle in pregnancy from 92,925 women (26,27). The women were enrolled between 1996 and 2002 in early pregnancy by their general practitioner, and approximately 60% of the invited women accepted to participate. The women completed telephone interviews twice in pregnancy and at approximately 6 and 18 months postpartum. Detailed information on the DNBC can be found elsewhere (26,27). Seven years after childbirth, the mothers were invited to complete a web-based or mailed follow-up questionnaire, which included information on weight and waist circumference. Finally, from January 2013 to January 2015, on average 14 years after childbirth, a follow-up study was conducted on mothers focusing on mental, physical and occupational health. The women

also provided information on weight parameters during their childbearing years and at the time of the follow-up.

We restricted the study to women who participated in the cohort with their first live birth and provided information on pre-pregnancy BMI ( $n=42,124$ ) (Figure 1). Of these, 21,060 women (50.0%) replied to the Maternal Follow-up questionnaire, and 18,349 (43.6%) had complete information on weight during the follow-up period. We excluded 153 women (0.8%) who were pregnant at the time of the follow-up. Also, we excluded 1,198 women (6.6%), who prior to the first pregnancy had a hospital diagnosis of any affective disorder (by ICD8 code 296 or ICD10 codes F30-39) or reported to have suffered from any psychological condition before being enrolled in DNBC in order to identify a cohort of mentally healthy women at baseline. The final study population included 16,998 mothers.



**Figure 1** Flowchart of the study population from the Danish National Birth Cohort (DNBC). BMI, body mass index.

## Exposures and outcomes

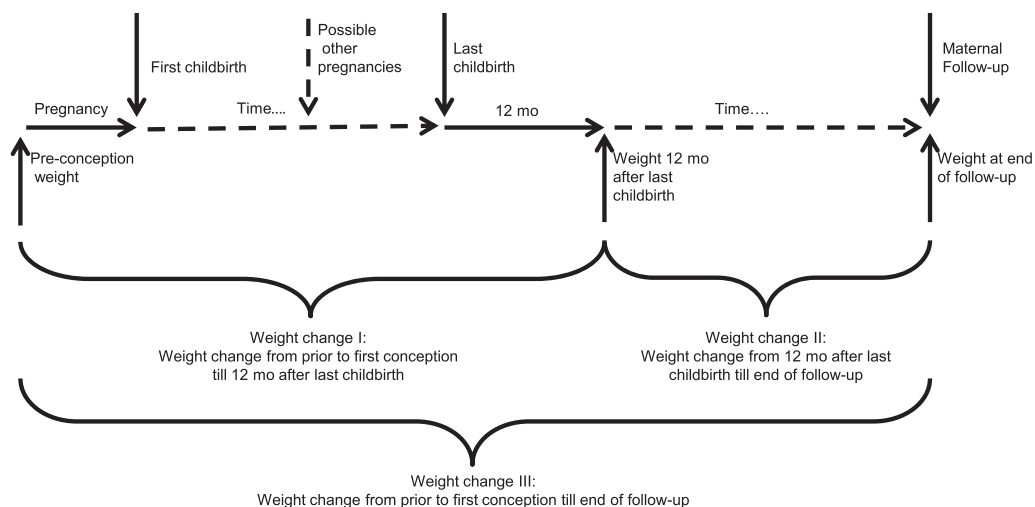
While recognizing the complex, possibly bi-directional, relations between body weight and depressive symptoms, we defined the body weight-related variables as exposures and the depressive symptoms as outcomes for analytical purposes. We report statistical associations knowing that the direction of associations remain unclear and further studies on causal directions are needed.

Pre-pregnancy BMI was calculated from self-reported pre-pregnancy weight and height, which were obtained during the first interview in the DNBC at approximately the 17th week. The BMI were categorized according to the World Health Organization classification as underweight ( $<18.5 \text{ kg m}^{-2}$ ), normal-weight ( $18.5\text{--}24.99 \text{ kg m}^{-2}$ ), overweight ( $25\text{--}29.99 \text{ kg m}^{-2}$ ) and obesity ( $\geq 30 \text{ kg m}^{-2}$ ) (28).

Next, we identified weight changes in different periods (Figure 2). (i) Weight change across years of childbearing, defined as weight change from before the pregnancy leading to the first live birth until 12 months after the last live birth in the follow-up period (childbearing-related weight change); (ii) weight change after the childbearing period, defined as weight change from 12 months after the last live birth till the time of the follow-up questionnaire (weight change after childbearing); and (iii) overall weight change, defined as weight change from prior to the pregnancy leading to the first live birth till the time of the follow-up questionnaire (total weight change). BMI at the end of each time period were calculated from self-reported weights in the Maternal Follow-up questionnaire. For all periods, weight changes were calculated as differences between BMI values at the start and the end of the specific period, and

categorized as weight loss ( $>1 \text{ kg m}^{-2}$ ), unchanged weight (between  $-1.00$  and  $0.99 \text{ kg m}^{-2}$ ), weight gain  $1\text{--}1.99 \text{ kg m}^{-2}$ , weight gain  $2\text{--}2.99 \text{ kg m}^{-2}$  and finally weight gain  $\geq 3 \text{ kg m}^{-2}$  (29). One BMI unit is equivalent to approximately 3 kg for a 168-cm-tall woman. Additionally, we categorized weight changes in three categories as those with the highest weight loss (10th percentile), those with the highest weight gain (90th percentile) and those with more moderate changes in weight (11–89th percentile).

Finally, we included waist circumference (cm) adjusted for BMI ( $\text{WC}_{\text{BMI}}$ , cm) as an exposure. In the 7-year follow-up questionnaire, women were instructed to measure WC at the narrowest point in centimetres with a mailed tape measure. We therefore excluded mothers with missing information on weight or WC from the 7-years questionnaire as well as women with this measure affected by an on-going or recent pregnancy (from conception through 12 months postpartum) for this analysis, leaving 11,290 (66.4%) women. As a measure of abdominal adiposity, we used the deviation from the value predicted by the BMI value estimated by the regression of WC on BMI. This measure indicates the variation in abdominal fatness that cannot be ascribed to variation in general adiposity measured by BMI (15), and even a woman with a low BMI can have positive values if her WC is larger than expected for her BMI. At the 7-year follow-up, the predicted waist circumference was 81.6 cm for a mean BMI at 7 years postpartum of  $23.0 \text{ kg m}^{-2}$ , and it increased by 2.15 cm for each increase in BMI unit. These data were used both as continuous variables and as categorical variables (divided in three equally sized groups;  $<-2.5$ ,  $-2.5\text{--}2.2$  and  $>2.2$  cm from the WC predicted by the BMI).



**Figure 2** Time line indicating time points for generation of weight change parameters.

The outcome measure 'depressive symptoms' was based on self-reported data from the Maternal Follow-up study, using the Center of Epidemiologic Studies Depression Scale Short (CES-D10) (30). The participants answered 10 questions about their mental status within the last week prior to filling the questionnaire, and each answer was given a score between 0 (rarely) and 3 (most of the time/always). The maximum sum of scores was 30, and scores  $\geq 10$  indicated depressive symptoms (30). The CES-D10 scale is a short version of the CES-D scale (31) developed by Radloff in 1977 to measure depressive symptomatology in the general population (30). It has been found to be a reliable and valid instrument for detecting major depressive disorders (32). The short version of the scale has a good predictive accuracy compared with the full-length version (31,33), and with a cut-off at 10, it has a high sensitivity for diagnostic performance (33,34). Thus, although a score of 10 or above does not need to reflect a psychiatric diagnosis of depression, the cut-off indicates more severe depressive symptoms.

## Covariates

From the baseline interview, we had information about socio-occupational status based on type of job or type of education if still attending school. Women in management or in jobs requiring higher education were categorized as 'high'. Office workers, service worker, skilled manual workers and women in the military constituted the 'middle' category. The category 'low' included unskilled workers and unemployed women (35). From the interviews 6 and 18 months postpartum, we had information on total weeks of breastfeeding (<20, 20–39 and 40+ weeks). The Maternal Follow-up questionnaire included information on smoking history, which was categorized as never, previous and current smokers. Information on parity at the end of follow-up was included in the Maternal Follow-up questionnaire, and was categorized as parity 1, 2 and 3+. Further, we adjusted for marital status (cohabitant/married or single) and place of residency (capital, cities >100,000 inhabitants or smaller cities/rural areas) at baseline.

In relation to the index pregnancy (at approximately gestational week 30 and 6 months postpartum), 12,732 women in the study population had answered three questions on actual depressive symptoms from the Symptoms Checklist-92 (36,37). Each of these could be answered with 'no'=1, 'a little'=2 and 'a lot'=3. The scores of the three questions (range 3–9) were added up, and two groups were generated (women without depressive symptoms [sum <5] and women with

depressive symptoms [sum  $\geq 5$ ] at the respective points in time). The cut-off was population specific and identified 13.5% and 13.7% as having depressive symptoms in mid-pregnancy and in early motherhood, respectively.

## Statistical analysis

The prevalence of depressive symptoms and prevalence differences according to each category of exposures were calculated, and logistic regression models were used to estimate odds ratios (OR) for the association between pre-pregnancy BMI, weight changes,  $WC_{BMI}$  at 7 years postpartum and self-reported depressive symptoms in midlife ( $CES-D10 \geq 10$ ). We adjusted for age at beginning of the first pregnancy, socio-occupational status, marital status and living area in pregnancy, as well as smoking history. In the analysis on weight change after the childbearing years and depressive symptoms, we included parity but not weight change in the previous time period. In the adjusted analyses of weight changes and depressive symptoms, we also included pre-pregnancy BMI. Potential confounders were chosen *a priori* and assessed by use of directed acyclic graphs (38). As time in the cohort may potentially affect the estimates, we added an interaction term indicating weight change in a short or long period (defined by under/over median time in the cohort) to all covariates in the analysis. Results indicated no statistically significant difference in estimates (results not shown).

We generated restricted cubic splines with six knots for the association between the selected weight parameters as continuous variables and depressive symptoms (Figure S1). Because some of these splines indicated U-shaped associations, we also estimated the linear association between continuous weight changes in strata of women who lost or gained weight and women with positive and negative  $WC_{BMI}$  and depressive symptoms (Table S1). The linear association between pre-pregnancy BMI >21 units and depressive symptoms were also estimated (Table S1). To adjust in part for reverse causation and to examine bi-directionality, we repeated the analyses adjusted for depressive symptoms in the beginning of the period under study (in gestational week 30 and/or 6 months postpartum, respectively) in mothers who had given the information ( $N = 12,732$ ) (Supplementary Table S2). Finally, to examine the robustness of the associations, we made the analyses with a CES-D score cut-off of 12 (Table S3). Results are presented as estimates with 95% confidence intervals (95% CI). Analyses were performed using STATA 13.0 (StatCorp, College Station, TX, USA).



## Results

Of the 16,998 first-time mothers in this study, 13.9% ( $n = 2,363$ ) reported to have depressive symptoms at the time of the Maternal Follow-up as indicated by a CES-D10 score  $\geq 10$  with a median score of 13 points (interquartile range [IQR] 11–16 points). Using a cut-off  $\geq 12$ , 8.7% of mothers had depressive symptoms. Median age at maternal follow-up was 42 years (IQR 40–45 years), and median time of follow-up was 14.3 years (IQR 13.2–15.2 years). In the 10th percentile with the highest weight loss, the median loss was  $2.4 \text{ kg m}^{-2}$  (IQR  $3.6\text{--}1.8 \text{ kg m}^{-2}$ ), and in the 90th percentile with the highest gain, the median weight gain was  $6.1 \text{ kg m}^{-2}$  (IQR  $5.2\text{--}7.7 \text{ kg m}^{-2}$ ). Compared with women without depressive symptoms at the time of the Maternal Follow-up, women with depressive symptoms were more likely to have a low socio-occupational status, to smoke at the time of the Maternal Follow-up, to be the mother of only one child, to have breastfed for a shorter period and to live alone (Table 1). Pre-pregnancy BMI tended to be higher for women with lower socio-occupational status and among current smokers. Total weight gain was lowest in women with high socio-occupational status, never smokers and mothers, who had three or more children.

### Pre-pregnancy body mass index

In the crude analysis of pre-pregnancy BMI, mothers with underweight, overweight and obesity all had more depressive symptoms at follow-up than normal-weight mothers. The adjusted analysis changed the estimates very little showing ORs for depressive symptoms of 1.29 (95% CI 0.99–1.68) for underweight mothers, 1.24 (95% CI 1.08–1.42) for mothers with overweight and 1.73 (95% CI 1.43–2.10) for women with obesity. The estimated association was j-shaped as also shown in Figure 3 with the lowest prevalence of depressive symptoms seen in women with a BMI of approximately 21.0. When restricting the analysis to women with a pre-pregnancy BMI  $> 21$ , the OR for depressive symptoms was 1.04 (95% CI 1.03–1.05) for every one unit increase in BMI when compared with a BMI 21 (Table S1).

### Childbearing-related weight changes

The odds of depressive symptoms in midlife increased with increasing weight gain in the years of childbearing. Thus, the adjusted ORs were 1.12 (95% CI 0.96–1.30) for women gaining  $1\text{--}1.99 \text{ kg m}^{-2}$ , 1.28 (95% CI 1.07–1.52) for women gaining  $2\text{--}2.99 \text{ kg m}^{-2}$  and 1.45 (95% CI 1.24–1.70) for women gaining 3 or more  $\text{kg m}^{-2}$ ,

indicating a linear trend among those gaining weight ( $p < 0.001$ ). Weight loss in this period was not associated with greater odds of depressive symptoms at follow-up than for women with no weight change.

### Weight changes after childbearing

All weight changes – both weight loss and gain – after the years of childbearing were associated with increased odds of depressive symptoms by the time of the Maternal Follow-up compared with maintaining a stable weight. After adjustment for potential confounders, weight loss was associated with a greater OR of 1.38 (95% CI 1.20–1.60) than no weight change. Across all categories of weight gain, ORs for depressive symptoms increased with increasing weight gain; the highest OR (1.88, 95% CI 1.58–2.22) was found in women who had a weight gain of  $3 \text{ kg m}^{-2}$  or more compared with women with no weight gain. There was a linear trend among those gaining weight ( $p < 0.001$ ).

### Total weight change

For the combined time period, weight changes of 2 or more  $\text{kg m}^{-2}$  were associated with increasing odds of depressive symptoms compared with no weight change with odds ratios of 1.11 (95% CI 0.92–1.33) and 1.68 (95% CI 1.46–1.94) for weight gains of  $2\text{--}2.99$  and  $3 + \text{kg m}^{-2}$ , respectively.

For all of the aforementioned analyses on weight changes, findings were corroborated on continuous data in Figure 3 and Table S1.

### The upper and lower 10th percentile weight changes

Across the entire time period, greater odds of depressive symptoms were observed in women with the highest weight gain ( $\geq 90$ th percentile) with an OR of 1.86 (95% CI 1.60–2.18) compared with women with smaller differences in weight change (the 11th–89th percentile). For those with the largest weight loss ( $\leq 10$ th percentile), the adjusted OR was 1.11 (95% CI 0.92–1.33).

### Waist circumference

Women who had a  $\text{WC}_{\text{BMI}} > 2.2 \text{ cm}$  7 years postpartum had a crude OR for depressive symptoms at follow-up of 1.21, which was unchanged after adjustment (OR of 1.16, 95% CI 0.99–1.36), compared with women with a  $\text{WC}_{\text{BMI}}$  between  $-2.5$  and  $2.2 \text{ cm}$  (Table 2). Women with a  $\text{WC}_{\text{BMI}} < -2.5 \text{ cm}$  showed a marginally increased OR of 1.09 (95% CI 0.93–1.28). A restricted cubic spline

**Table 1** Sample characteristics for all mothers and mothers with depressive symptoms in midlife from the Danish National Birth Cohort (*n* = 16,998)

	Study population		BMI	(IQR)	WCIII	(IQR)	Depressive symptoms		No depressive symptoms	
Study population	16,998	100.0%	22.39	(20.62–24.80)	1.03	(–0.00–2.54)	2,363	13.9%	14,635	86.1%
Age, median (IQR) years										
At baseline	28.0	(25.9–30.6)					28.1	(25.7–30.9)	28.0	(25.9–30.5)
At end of follow-up	42.2	(40.0–45.0)					42.3	(39.9–45.3)	42.2	(40.0–44.9)
Social status %										
Low	842	5.0%	22.85	(20.57–26.22)	1.63	(0.00–3.59)	161	6.8%	681	4.7%
Middle	5,354	31.5%	22.84	(20.82–25.47)	1.26	(–0.00–2.99)	819	34.7%	4,535	31.0%
High	10,473	61.6%	22.20	(20.55–24.38)	0.78	(–0.32–2.21)	1,311	55.5%	9,162	62.6%
Smoking history %										
Never smoker	9,501	55.9%	22.32	(20.58–24.80)	1.00	(–0.00–2.42)	1,173	49.6%	8,328	56.9%
Former smoker	5,707	33.6%	22.32	(20.62–24.61)	1.06	(–0.00–2.70)	829	35.1%	4,878	33.3%
Smoker	1,458	8.6%	22.85	(20.76–25.69)	1.06	(–0.37–3.01)	316	13.4%	1,142	7.8%
Children during reproductive period %										
1	2,608	15.3%	22.60	(20.76–25.43)	1.19	(0.00–2.90)	427	18.1%	2,181	14.9%
2	9,731	57.2%	22.41	(20.66–24.80)	1.03	(–0.30–2.50)	1,348	57.0%	8,383	57.3%
3+	4,659	27.4%	22.21	(20.53–24.46)	0.96	(–0.29–2.42)	588	24.9%	4,071	27.8%
Habitant status										
Married or cohabitant	16,671	98.1%	22.39	(20.62–24.80)	1.01	(–0.00–2.51)	2,294	97.1%	14,377	98.2%
Single	317	1.9%	22.50	(20.57–24.69)	1.84	(0.39–4.63)	68	2.9%	249	1.7%
Living area										
Capital	2,897	17.0%	21.63	(20.18–23.66)	0.89	(0.00–2.13)	413	17.5%	2,484	17.0%
City of >100,000 inhabitants	2,584	15.2%	22.13	(20.55–24.22)	0.95	(–0.33–2.34)	328	13.9%	2,256	15.4%
Smaller cities or rural areas	11,517	67.8%	22.66	(20.76–25.26)	1.06	(–0.00–2.70)	1,622	68.6%	9,895	67.6%
Breastfeeding										
<20 weeks	3,161	18.6%	23.24	(21.08–26.40)	1.21	(–0.32–3.19)	509	21.5%	2,652	18.1%
20–39 weeks	5,908	34.8%	22.27	(20.57–24.51)	0.97	(–0.00–2.31)	738	31.2%	5,170	35.3%
40+ weeks	3,629	21.3%	22.03	(20.45–24.16)	0.93	(–0.00–2.31)	460	19.5%	3,169	21.7%
Time in intervals, median (IQR) y										
Pre-conception – 12 months after last birth	4.9	(3.7–6.9)					4.9	(3.6–7.0)	4.9	(3.8–6.9)
12 months after last birth – Maternal follow-up	9.1	(7.1–10.9)					9.2	(7.1–11.1)	9.1	(7.1–10.9)
Pre-conception – Maternal follow-up	14.3	(13.2–15.2)					14.5	(13.4–15.3)	14.3	(13.2–15.2)
Anthropometrics										
Pre-pregnancy BMI, median (IQR) BMI units	22.4	(20.6–24.8)					22.8	(20.8–25.6)	22.3	(20.6–24.7)
Weight change I, median (IQR) BMI units	0.7	(–0.4–2.0)					0.8	(–0.4–2.4)	0.7	(–0.4–2.0)
Weight change II, median (IQR) BMI units	0.4	(–0.7–1.6)					0.7	(–0.7–2.2)	0.3	(–0.7–1.5)
Weight change III, median (IQR) BMI units	1.0	(–0.0–2.5)					1.4	(0.0–3.5)	1.0	(–0.0–2.4)
Waist circumference at 7 years, median (IQR) cm	82.0	(76.0–89.0)					83.0	(77.0–91.0)	81.0	(76.0–88.0)

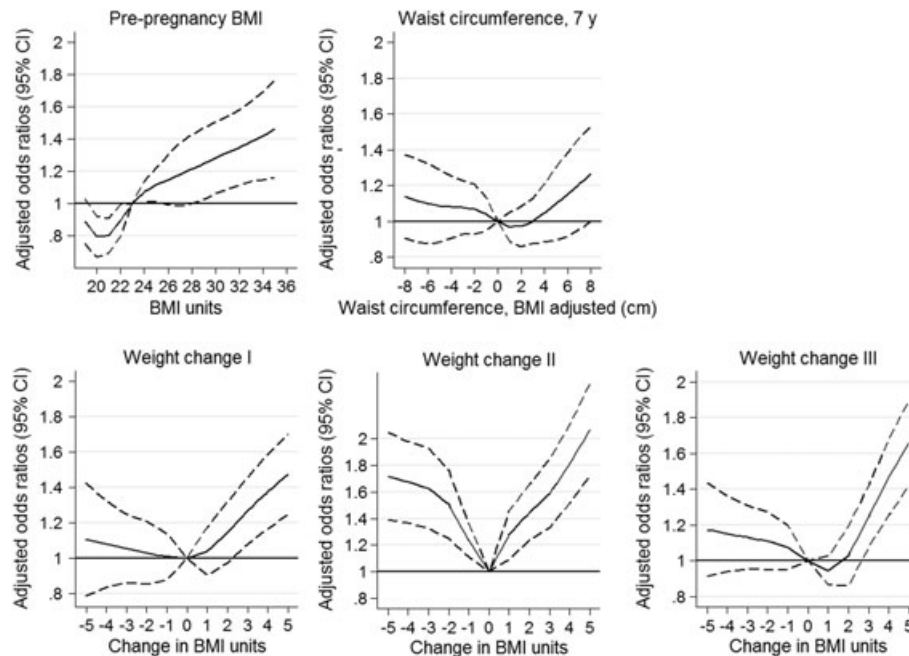
Weight change I: weight change from prior to conception of the first child till 12 months after last childbirth prior to the maternal follow-up.

Weight change II: weight change from 12 months after last childbirth prior to the maternal follow-up till the time of the maternal follow-up.

Weight change (WC) III: weight change from prior to conception of the first child till the time of the maternal follow-up.

All columns do not sum up to 100% because of missing data.

BMI, body mass index; IQR, interquartile range.



**Figure 3** Logistic regression for self-reported depressive symptoms (Center of Epidemiologic Studies Depression Scale Short, score  $\geq 10$ ) according to different weight parameters and BMI-adjusted waist circumference in first-time mothers in the Danish National Birth Cohort. Restricted cubic splines adjusted for smoking, social status, age, breastfeeding, marital status and place of residency during pregnancy. Weight change estimates also adjusted for pre-pregnancy BMI as well as weight change III is adjusted for parity. Weight change I: weight change from pre-conception till 12 months after last childbirth. Weight change II: weight change from 12 months after last childbirth till the time of the Maternal Follow-up. Weight change III: weight change from pre-conception till the time of the Maternal Follow-up. The dotted lines show 95% confidence intervals. BMI, body mass index.

showed a linear association from  $WC_{BMI}$  of 0.0 cm and upwards (Figure 3), which is presented in Table S1, indicating a greater OR of 1.04 (95% CI 1.02–1.07) for each 1-cm increase in  $WC_{BMI}$ .

When applying a cut-off of  $\geq 12$  as definition of depressive symptoms, results supported the main findings although associations for some analyses were stronger (Table S3). Adding adjustment for depressive symptoms measured close to baseline in relation to the index pregnancy did only alter results a little (differences in OR between  $-0.09$  and  $+0.04$ ) (Table S2).

## Discussion

We found that low and high pre-pregnancy BMI, weight loss after years of childbearing and weight gain, both in the childbearing years and particular in the years after the last childbirth, were associated with depressive symptoms among mothers in midlife 11–16 years after childbirth. Further, women with a larger WC than predicted by their BMI, indicating a relative excess of abdominal fat mass, reported more depressive symptoms than women with a WC in accordance with their BMI.

Many women experience depressive symptoms in midlife (20), and mother's well-being is of importance

not only to themselves but also their families and society. Our results indicate an association between weight, weight changes and depressive symptoms, which suggest that health professionals should pay attention to mothers who retain larger weight changes in their reproductive years and beyond as these weight changes may be associated with depressive symptoms. Likewise, they should also pay attention to women with depressive symptoms as they may be more susceptible to weight change.

Our results are in accordance with results from the general population on obesity and depression (5,6,39). In analyses focusing on women only, obesity was also associated with a greater risk of later depressive symptoms with a relative increased risk of 10–33% compared with normal-weight women (7,8,40). We found an OR of 1.73 for women with obesity, indicating an even higher excess risk of depressive symptoms in our cohort of mothers. In a former study based on the DNBC, we found no increased risk for anxiety and/or depression in mothers with obesity over a 6-year period (13). The outcome was defined by redeemed prescriptions and/or ICD10 codes, which might explain the differences. In the present study, we capture signs of depression, which may not be so severe that it leads to a prescription or



**Table 2** Odds ratios (OR) for self-reported depressive symptoms (CES-D  $\geq 10$ ) according to pre-pregnancy BMI and different weight parameters in the Danish National Birth Cohort ( $N = 16,998$ )

	<i>N</i>	Depressive symptoms	%	PD (%)	OR Crude	OR Adjust*	(95% CI)	OR Adjust**	(95% CI)
<b>Pre-pregnancy BMI</b>									
Underweight	627	103	16.4	3.7	1.35	1.29	(0.99–1.68)	NA	—
Normal-weight	12,376	1,576	12.7	0.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)	—	NA	—
Overweight	2,959	473	16.0	3.3	1.30	1.24	(1.08–1.42)	NA	—
Obese	1,036	211	20.4	7.7	1.75	1.73	(1.43–2.10)	NA	—
<b>Childbearing-related weight change (BMI units)</b>									
Loss of >1	2,724	393	14.4	1.9	1.19	1.13	(0.97–1.33)	1.03	(0.87–1.21)
–1–0.99	6,714	836	12.5	0.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)	—	1.0 (Ref.)	—
1–1.99	3,299	424	12.9	0.4	1.04	1.11	(0.96–1.29)	1.12	(0.96–1.30)
2–2.99	1,784	261	14.6	2.1	1.20	1.29	(1.08–1.54)	1.28	(1.07–1.52)
3+	2,477	449	18.1	6.3	1.56	1.53	(1.31–1.79)	1.45	(1.24–1.70)
<b>Weight change after childbearing (BMI units)</b>									
Loss of >1	3,619	538	14.9	3.8	1.40	1.46	(1.27–1.68)	1.38	(1.20–1.60)
–1–0.99	7,544	836	11.1	0.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)	—	1.0 (Ref.)	—
1–1.99	2,507	356	14.2	3.1	1.33	1.27	(1.08–1.50)	1.26	(1.07–1.48)
2–2.99	1,462	223	15.3	4.2	1.44	1.39	(1.15–1.69)	1.35	(1.11–1.64)
3+	1,866	410	22.0	10.9	2.26	2.00	(1.70–2.37)	1.88	(1.58–2.22)
<b>Total weight change (BMI units)</b>									
Loss of >1	2,355	337	14.3	2.6	1.26	1.28	(1.08–1.51)	1.14	(0.96–1.36)
–1–0.99	5,974	700	11.7	0.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)	—	1.0 (Ref.)	—
1–1.99	3,233	367	11.4	–0.3	0.96	0.98	(0.84–1.15)	0.99	(0.84–1.16)
2–2.99	1,972	281	14.2	2.5	1.25	1.11	(0.92–1.34)	1.11	(0.92–1.33)
3+	3,464	678	19.6	7.9	1.83	1.75	(1.52–2.02)	1.68	(1.46–1.94)
<b>Extreme changes, whole period</b>									
10% with greatest weight loss	1,699	254	14.9	2.3	1.22	1.26	(1.06–1.49)	1.11	(0.92–1.33)
No extreme changes	13,599	1,713	12.6	0.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)	—	1.0 (Ref.)	—
10% with greatest weight gain	1,700	396	23.3	10.7	2.11	1.97	(1.69–2.29)	1.86	(1.60–2.18)
<b>BMI-adjusted waist circumference, 7 years (cm)</b>									
<–2.5 cm	3,762	506	13.5	1.8	1.18	1.09	(0.93–1.28)	NA	—
–2.5–2.2	3,764	439	11.7	0.0 (Ref.)	1.0 (Ref.)	1.0 (Ref.)	—	NA	—
>2.2	3,764	519	13.8	2.1	1.21	1.16	(0.99–1.36)	NA	—

\*Adjusted for social status, smoking, age, breastfeeding, marital status and living area. Weight change after childbearing (WCII) also adjusted for parity.

\*\*Additionally adjusted for pre-pregnancy BMI.

BMI, body mass index; *N*, numbers; PD, prevalence difference; OR, odds ratio; CI, confidence intervals.

diagnosis, but indicate poor mental well-being in women with high pre-pregnancy BMI. In both studies, being underweight was associated with a greater risk of poor mental health. It may also be that the behaviour of the health professionals can explain these differences if they are more alert to underweight women with depressive symptoms. Further, underweight may be a sign of underlying conditions such as anorexia or chronic diseases that may also affect mental health (41–43).

The higher prevalence of depressive symptoms in mothers with weight gain compared with mothers with a stable weight is in line with previous follow-up studies, which found that mental well-being was highest in women with a stable weight during a 2-year period in midlife (44), while women who lost weight or gained more than 10% of their BMI over a 3-year period had an elevated risk of clinically significant depressive symptoms (8). In a cohort study surveying women on weight and depression scores

every third year in a 12-year period, weight change and depression were also associated, but after using weight change in the two preceding surveys as a predictor for depression, the association disappeared (12). Other studies have found that depressive conditions may lead to weight changes – both loss and gain, (12,45–49) supporting the idea that effects of weight change and depressive symptoms may be bi-directional and associations intertwined.

Irrespective of the temporal relations between body weight measures and depressive symptoms in the present study, the causal direction cannot be determined. Because of the long time span in our cohort, depressive symptoms in each mother may have come and gone more than once during follow-up and affected weight changes. Clearly, we report a point prevalence of depressive symptoms in midlife. We had sparse information about depressive symptoms during follow-up to examine bi-directionality, but when adjusting for depressive symptoms at gestational week 30 and 6 months postpartum in the beginning of the study period, it had little effect on our findings. The combination of results and consistency in associations suggest that weight gain or loss may affect symptoms of depression although reverse causation cannot be ruled out. Future research should study causality including direction and possible mechanisms of these associations.

We found increased  $WC_{BMI}$  to be associated with greater odds of depressive symptoms. This has not previously been studied in mothers but abdominal obesity has been linked with depression in men (4,23).

The main strength of this study pertains to the features of the DNBC, including the Maternal Follow-up, allowing for a large sample size with detailed information on potential confounders. With several weight measurements during follow-up, we were able to detect time periods of weight change and separate weight changes related to the childbearing period and beyond. Another important strength is the identification of self-reported depressive symptoms using a validated score and our ability to account for depressive disorders and depressive symptoms close to baseline.

This study also has some limitations. All exposure information on weight parameters and waist circumference in this study was self-reported. Thus, there is some misclassification. We know from a validation study within the DNBC (50) that pre-pregnancy BMI tended to be under-reported with approximately 0.6 kg, and this underreporting increased slightly with increasing BMI. However, agreement within BMI categories was approximately 90%. The weights for calculation of the respective weight changes may suffer from similar under-reporting, which may attenuate the error on weight changes

measures. The mothers had to recall weight 12 months after last childbirth, which may be prone to errors. Reassuringly, when comparing reported weight at 18 months (from an interview at 18 months postpartum) and recalled weight 12 months after last childbirth in women with one child only, we found a high correlation in calculated BMI (Pearson's correlation = 0.89). We do not anticipate any systematic differential misclassification by level of depressive symptoms.

Of the initial eligible study population, only 51% participated in the Maternal Follow-up. Of these, some did not provide information on weight parameters during follow-up. Women with information on weight parameters were older at baseline, had a higher socio-occupational status and had a lower pre-pregnancy BMI than those not providing these data (data not shown). Also, weight gain during follow-up, family size and depressive symptoms status may be associated with non-participation and hence potentially lead to selection bias. However, by adjusting for factors such as age, socio-occupational status, smoking, marital status and parity, which may be associated with both participation and depressive symptoms, we aimed to reduce the influence from selection bias (51). Despite adjustment for potential confounders, we cannot rule out risk of residual confounders due to unknown or unmeasured confounding. We had no data to adjust for chronic diseases and medication. Notably, the DNBC consists of Caucasian women only, and generalizability of our findings to other groups is unknown.

In conclusion, high and low pre-pregnancy BMI, weight gain during the years of childbearing and the following years, and abdominal obesity increased the prevalence of depressive symptoms in maternal midlife. These findings suggest having a healthy weight prior to reproduction and retaining this weight, except when pregnant, support mental well-being in mothers in midlife. Prevention of obesity and weight changes, other than gestational weight gain, may lead to less depressive symptoms in mothers in midlife.

## Conflict of interest statement

The authors declared no conflicts of interest.

## Funding

The Danish National Research Foundation established the Danish Epidemiology Science Centre, which initiated and created the Danish National Birth Cohort. The cohort is a result of a major grant from this Foundation. Additional support for the Danish National Birth Cohort was obtained from the Pharmacy Foundation, the Egmont Foundation, the March of Dimes Birth Defects Foundation

and the Augustinus Foundation. Support for the Maternal Follow-up was granted by The Danish Council for Independent Research (0602-01042B).

## References

1. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980–2013: a systematic analysis for the Global Burden of Disease Study 2013. *Lancet Lond Engl* 2014; **384**: 766–781.
2. Data Sundhedsstyrelsen. Esundhed.dk. [WWW document]. URL <http://www.esundhed.dk/sundhedsregistre/MFR/Sider/MFR06A.aspx>
3. Mladovsky P, European Observatory on Health Systems and Policies, World Health Organization. *Health in the European Union: Trends and Analysis*. Copenhagen: World Health Organization on behalf of the European Observatory on Health Systems and Policies, 2009.
4. Vogelzangs N, Kritchevsky SB, Beekman ATF, et al. Obesity and onset of significant depressive symptoms: results from a prospective community-based cohort study of older men and women. *J Clin Psychiatry* 2010; **71**: 391–399.
5. Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry* 2010; **67**: 220–229.
6. de Wit L, Luppino F, van Straten A, Penninx B, Zitman F, Cuijpers P. Depression and obesity: a meta-analysis of community-based studies. *Psychiatry Res* 2010; **178**: 230–235.
7. Pan A, Sun Q, Czernichow S, et al. Bidirectional association between depression and obesity in middle-aged and older women. *Int J Obes* 2005 2012; **36**: 595–602.
8. Ball K, Burton NW, Brown WJ. A prospective study of overweight, physical activity, and depressive symptoms in young women. *Obes Silver Spring Md* 2009; **17**: 66–71.
9. Allison DB, Newcomer JW, Dunn AL, et al. Obesity among those with mental disorders: a National Institute Of Mental Health meeting report. *Am J Prev Med* 2009; **36**: 341–350.
10. Molyneaux E, Poston L, Ashurst-Williams S, Howard LM. Obesity and mental disorders during pregnancy and postpartum: a systematic review and meta-analysis. *Obstet Gynecol* 2014; **123**: 857–867.
11. LaCoursiere DY, Barrett-Connor E, O'Hara MW, Hutton A, Varner MW. The association between prepregnancy obesity and screening positive for postpartum depression. *BJOG Int J Obstet Gynaecol* 2010; **117**: 1011–1018.
12. Singh G, Jackson CA, Dobson A, Mishra GD. Bidirectional association between weight change and depression in mid-aged women: a population-based longitudinal study. *Int J Obes* 2005; **2013**.
13. Bliddal M, Pottegård A, Kirkegaard H, et al. Mental disorders in motherhood according to prepregnancy BMI and pregnancy-related weight changes – a Danish cohort study. *J Affect Disord* 2015; **183**: 322–329.
14. Gunderson EP, Abrams B. Epidemiology of gestational weight gain and body weight changes after pregnancy. *Epidemiol Rev* 2000; **22**: 261–274.
15. Kirkegaard H, Stovring H, Rasmussen KM, Abrams B, Sorensen TI, Nohr EA. How do pregnancy-related weight changes and breastfeeding relate to maternal weight and BMI-adjusted waist circumference 7 y after delivery? Results from a path analysis. *Am J Clin Nutr* 2013. DOI: 10.3945/ajcn.113.067405.
16. Nehring I, Schmoll S, Beyerlein A, Hauner H, von Kries R. Gestational weight gain and long-term postpartum weight retention: a meta-analysis. *Am J Clin Nutr* 2011; **94**: 1225–1231.
17. Mannan M, Doi SA, Mamun AA. Association between weight gain during pregnancy and postpartum weight retention and obesity: a bias-adjusted meta-analysis. *Nutr Rev* 2013; **71**: 343–352.
18. Herring SJ, Rich-Edwards JW, Oken E, Rifas-Shiman SL, Kleinman KP, Gillman MW. Association of postpartum depression with weight retention 1 year after childbirth. *Obes Silver Spring Md* 2008; **16**: 1296–1301.
19. Penninx BWJH, Milaneschi Y, Lamers F, Vogelzangs N. Understanding the somatic consequences of depression: biological mechanisms and the role of depression symptom profile. *BMC Med* 2013; **11**: 129.
20. van Uffelen JGZ, van Gellecum YR, Burton NW, Peeters G, Heesch KC, Brown WJ. Sitting-time, physical activity, and depressive symptoms in mid-aged women. *Am J Prev Med* 2013; **45**: 276–281.
21. Gunderson EP, Sternfeld B, Wellons MF, et al. Childbearing may increase visceral adipose tissue independent of overall increase in body fat. *Obes Silver Spring Md* 2008; **16**: 1078–1084.
22. Vogelzangs N, Kritchevsky SB, Beekman ATF, et al. Depressive symptoms and change in abdominal obesity in older persons. *Arch Gen Psychiatry* 2008; **65**: 1386–1393.
23. Herva A, Laitinen J, Miettinen J, et al. Obesity and depression: results from the longitudinal Northern Finland 1966 Birth Cohort Study. *Int J Obes* 2005 2006; **30**: 520–527.
24. Penninx BWJH, Kritchevsky SB, Yaffe K, et al. Inflammatory markers and depressed mood in older persons: results from the Health, Aging and Body Composition study. *Biol Psychiatry* 2003; **54**: 566–572.
25. Park HS, Park JY, Yu R. Relationship of obesity and visceral adiposity with serum concentrations of CRP, TNF-alpha and IL-6. *Diabetes Res Clin Pract* 2005; **69**: 29–35.
26. Olsen J, Melbye M, Olsen SF, et al. The Danish National Birth Cohort – its background, structure and aim. *Scand J Public Health* 2001; **29**: 300–307.
27. Statens Serum Institut. Bedre Sundhed for Mor Og Barn. [www.bsig.dk](http://www.bsig.dk).
28. World Health Organization. *Preventing and Managing the Global Epidemic*. World Health Organization: Geneva, Switzerland, 2000.
29. Villamor E, Cnattingius S. Interpregnancy weight change and risk of adverse pregnancy outcomes: a population-based study. *Lancet Lond Engl* 2006; **368**: 1164–1170.
30. Radloff L. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas* 1977; **1**: 385–401.
31. Andresen EM, Malmgren JA, Carter WB, Patrick DL. Screening for depression in well older adults: evaluation of a short form of the CES-D (Center for Epidemiologic Studies Depression Scale). *Am J Prev Med* 1994; **10**: 77–84.
32. Beekman AT, Deeg DJ, Van Limbeek J, Braam AW, De Vries MZ, Van Tilburg W. Criterion validity of the Center for Epidemiologic Studies Depression scale (CES-D): results from a community-based sample of older subjects in the Netherlands. *Psychol Med* 1997; **27**: 231–235.
33. Cheng S-T, Chan ACM. The Center for Epidemiologic Studies Depression Scale in older Chinese: thresholds for long and short forms. *Int J Geriatr Psychiatry* 2005; **20**: 465–470.

34. Boey KW. Cross-validation of a short form of the CES-D in Chinese elderly. *Int J Geriatr Psychiatry* 1999; **14**: 608–617.
35. Nohr EA, Bech BH, Davies MJ, Frydenberg M, Henriksen TB, Olsen J. Prepregnancy obesity and fetal death: a study within the Danish National Birth Cohort. *Obstet Gynecol* 2005; **106**: 250–259.
36. Derogatis LR. *SCL-90-R: Administration, Scoring & Procedures Manual - II for the R(evised) Version and Other Instruments of the Psychopathology Rating Scale Series*, 2nd edn. Clinical psychometric research, inc.: Towson, Md., 1992.
37. Olsen LR, Mortensen EL, Bech P. The SCL-90 and SCL-90R versions validated by item response models in a Danish community sample. *Acta Psychiatr Scand* 2004; **110**: 225–229.
38. Shrier I, Platt RW. Reducing bias through directed acyclic graphs. *BMC Med Res Methodol* 2008; **8**: 70.
39. Atlantis E, Baker M. Obesity effects on depression: systematic review of epidemiological studies. *Int J Obes* 2005 2008; **32**: 881–891.
40. Bjerkeset O, Romundstad P, Evans J, Gunnell D. Association of adult body mass index and height with anxiety, depression, and suicide in the general population: the HUNT study. *Am J Epidemiol* 2008; **167**: 193–202.
41. Godart NT, Perdereau F, Rein Z, et al. Comorbidity studies of eating disorders and mood disorders. Critical review of the literature. *J Affect Disord* 2007; **97**: 37–49.
42. Liu B, Floud S, Pirie K, et al. Does happiness itself directly affect mortality? The prospective UK Million Women Study. *Lancet Lond Engl* 2016; **387**: 874–881.
43. Kim WK, Shin D, Song WO. Depression and its comorbid conditions more serious in women than in men in the United States. *J Womens Health* 2002 2015; **24**: 978–985.
44. Williams LT, Young AF, Brown WJ. Weight gained in two years by a population of mid-aged women: how much is too much? *Int J Obes* 2005 2006; **30**: 1229–1233.
45. de Wit LM, van Straten A, Lamers F, Cuijpers P, Penninx BWJH. Depressive and anxiety disorders: associated with losing or gaining weight over 2 years? *Psychiatry Res* 2015; **227**: 230–237.
46. Forman-Hoffman VL, Yankey JW, Hillis SL, Wallace RB, Wolinsky FD. Weight and depressive symptoms in older adults: direction of influence? *J Gerontol B Psychol Sci Soc Sci* 2007; **62**: S43–S51.
47. Koster A, van Gool CH, Kempen GJ, et al. Late-life depressed mood and weight change contribute to the risk of each other. *Am J Geriatr Psychiatry Off J Am Assoc Geriatr Psychiatry* 2010; **18**: 236–244.
48. Brumpton B, Langhammer A, Romundstad P, Chen Y, Mai X-M. The associations of anxiety and depression symptoms with weight change and incident obesity: the HUNT Study. *Int J Obes* 2005 2013; **37**: 1268–1274.
49. Pedersen P, Baker JL, Henriksen TB, et al. Influence of psychosocial factors on postpartum weight retention. *Obes Silver Spring Md* 2011; **19**: 639–646.
50. Nohr EA. Obesity in pregnancy. Epidemiological studies based on the Danish National Birth Cohort. Doctoral dissertation. Aarhus, Denmark: University of Aarhus, 2005.
51. Greene N, Greenland S, Olsen J, Nohr EA. Estimating bias from loss to follow-up in the Danish National Birth Cohort. *Epidemiol Camb Mass* 2011; **22**: 815–822.

## Supporting Information

### Figure S1.

**Supplementary Table S1.** Odd ratios (OR) for self-reported depressive symptoms according to weight changes in sub-groups of women with weight loss or gain or less or more abdominal fat mass than predicted. For women with BMI > 21 units: OR for self-reported depressive symptoms according to pre-pregnancy body mass index (BMI) on continuous data. First-time mothers in the Danish National Birth Cohort

**Supplementary Table S2.** Odds ratios (OR) for self-reported depressive symptoms (CES-D ≥ 10) according to pre-pregnancy BMI and different weight parameters in the Danish National Birth Cohort (N = 12,732). WITH ADJUSTMENT FOR DEPRESSIVE SYMPTOMS IN PREGNANCY AND 6 MONTHS AFTER CHILDBIRTH

**Supplementary Table S3.** Odds ratios (OR) for self-reported depressive symptoms (CESD-S ≥ 12) according to pre-pregnancy BMI and different weight parameters in the Danish National Birth Cohort (N = 16,998)